Transmission of Oscillatory Volumes into the Preterm Lung during Noninvasive High-Frequency Ventilation

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Abstract: Rationale: There is increasing evidence for a clinical benefit of noninvasive high-frequency oscillatory ventilation (nHFOV) in preterm infants. However, it is still unknown whether the generated oscillations are effectively transmitted to the alveoli. Objectives: To assess magnitude and regional distribution of oscillatory volumes (VOsc) at the lung level. Methods: In 30 prone preterm infants enrolled in a randomized crossover trial comparing nHFOV with nasal continuous positive airway pressure (nCPAP), electrical impedance tomography (EIT) recordings were performed. During nHFOV, the smallest amplitude to achieve visible chest wall vibration was used, and the frequency was set at 8 hertz (Hz). Measurements and main results: Thirty consecutive breaths during artefact-free tidal ventilation were extracted for each of the 228 EIT recordings. After application of corresponding frequency filters, tidal volumes (VT) and VOsc were calculated. There was a signal at 8 and 16 Hz during nHFOV which was not detectable during nCPAP, corresponding to the set oscillatory frequency and its second harmonic. During nHFOV, the mean (SD) VOsc/VT ratio was 0.20 (0.13). Oscillations were more likely to be transmitted to the non-gravity-dependent [mean difference (95% CI): 0.041 (0.025 to 0.058); $p<0.001$] and right-sided lung [mean difference (95% CI): 0.040 (0.019 to 0.061); $p<0.001$] when compared with spontaneous VT. Conclusions: In preterm infants, VOsc during nHFOV are transmitted to the lung. Compared with the regional distribution of tidal breaths, oscillations preferentially reach the right and non-gravity-dependent lung. These data increase our understanding of the physiological processes underpinning nHFOV and may lead to further refinement of this novel technique.

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Transmission of Oscillatory Volumes into the Preterm Lung during Noninvasive High-Frequency Ventilation

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At a Glance Commentary

Scientific Knowledge on the Subject

Noninvasive high-frequency oscillatory ventilation (nHFOV) is a relatively new technique designed to augment the effectiveness of nasal continuous positive airway pressure (nCPAP) in neonates. Current evidence suggests that nHFOV may be a promising alternative to other noninvasive modes for supporting ventilation and avoiding endotracheal intubation in preterm infants, although the mechanisms by which these clinical benefits are achieved are largely unknown.

What This Study Adds to the Field

This study provides first evidence of substantial transmission of oscillatory volumes into the lung of preterm infants on nHFOV support. Compared with the regional distribution of tidal breaths, oscillations are more likely to reach the right and the non-gravity-dependent areas of the lung.

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Abstract

Rationale:

There is increasing evidence for a clinical benefit of noninvasive high-frequency oscillatory ventilation (nHFOV) in preterm infants. However, it is still unknown whether the generated oscillations are effectively transmitted to the alveoli.

Objectives:

To assess magnitude and regional distribution of oscillatory volumes (V_{Osc}) at the lung level.

Methods:

In 30 prone preterm infants enrolled in a randomized crossover trial comparing nHFOV with nasal continuous positive airway pressure (nCPAP), electrical impedance tomography (EIT) recordings were performed. During nHFOV, the smallest amplitude to achieve visible chest wall vibration was used, and the frequency was set at 8 hertz (Hz).

Measurements and Main Results:

Thirty consecutive breaths during artefact-free tidal ventilation were extracted for each of the 228 EIT recordings. After application of corresponding frequency filters, tidal volumes (V_T) and V_{Osc} were calculated. There was a signal at 8 and 16 Hz during nHFOV which was not detectable during nCPAP, corresponding to the set oscillatory frequency and its second harmonic. During nHFOV, the mean (SD) V_{Osc}/V_T ratio was 0.20 (0.13). Oscillations were more likely to be transmitted to the non-gravity-dependent [mean difference (95% CI): 0.041 (0.025 to 0.058); p<0.001] and right-sided lung [mean difference (95% CI): 0.040 (0.019 to 0.061); p<0.001] when compared with spontaneous V_T.

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Conclusions:

In preterm infants, V_{Osc} during nHFOV are transmitted to the lung. Compared with the regional distribution of tidal breaths, oscillations preferentially reach the right and non-gravity-dependent lung. These data increase our understanding of the physiological processes underpinning nHFOV and may lead to further refinement of this novel technique.

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Introduction

The use of noninvasive high-frequency oscillatory ventilation (nHFOV) as respiratory support for preterm infants is increasing, due to potential benefits over the standard noninvasive respiratory support, nasal continuous positive airway pressure (nCPAP).(1–3) Clinical studies suggest that nHFOV may be superior to nCPAP for carbon dioxide (CO_2) clearance and may improve respiratory stability, particularly in preterm infants with evolving bronchopulmonary dysplasia.(4–7) However, the physiological effects within the lung accounting for these findings are poorly understood.

Due to the heterogeneous pattern of lung disease in these infants, ventilation distribution and regional lung volumes cannot be assumed to be uniform throughout all lung units, especially in gravity-dependent lung regions.(8, 9) This is particularly so during HFOV where ventilation is maintained using complex gas flow mechanisms.(10–13) Animal data during invasive (endotracheal) HFOV suggest that oscillations are shifted towards the non-gravity-dependent lung at higher frequencies.(14) During facemask-delivered nHFOV in one-year old infants, oscillations resulted in only marginal thoracic movements when measured with respiratory inductance plethysmography.(15) Since oscillations are known to be dampened by the ventilator circuit, the nasal interface and leaks around the nose and mouth, the magnitude and regional distribution of oscillatory volumes (V_{Osc}) that are actually transmitted to the alveoli remain unknown.(10–13, 15)

Conventional tools for monitoring the regional behavior of the neonatal lung expose the infant to radiation or procedures that are unacceptably invasive.(16) Electrical impedance tomography (EIT) is a noninvasive, radiation-free method that measures the regional ventilation distribution in a cross-sectional slice of the lung.(17) This continuous assessment

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of regional lung function has been shown to be representative of the whole lung in ventilated preterm infants.(18)

In the current study, EIT data from our randomized crossover trial on the effect of nHFOV on preterm infants were analyzed.(7) We tested the hypothesis that, in preterm infants born at <30 weeks of gestation, nHFOV would result in a significant transmission of V_{Osc} to the lungs. We speculated that V_{Osc} would be evenly distributed between the right and the left lung but greater in the non-gravity-dependent regions.

Methods

The trial was registered with the Australian and New Zealand Clinical Trials Registry (ACTRN12616001516471) and approved by the local ethics committee. All parents provided written informed consent.

Population and Intervention

Preterm infants born before 30 weeks' gestation who were 1) extubated for more than 24 hours, 2) older than 7 days, 3) between 26-34 completed weeks of gestation, and 4) clinically stable whilst receiving nCPAP support at the time of study were randomized to receive nHFOV or nCPAP first, each for 120 minutes. Infants were managed on the assigned therapy for an additional 30 minutes prior to each study period. This was considered a washout period and not included in the analysis. A Babylog VN500 ventilator (Dräger Medical System, Lübeck, Germany) and short binasal prongs (Hudson Respiratory Care, Temecula, California) were used for both intervention periods. The bias gas flow rate was 6 liters per minute. During the study, the nCPAP level (CPAP phase) and mean airway pressure (nHFOV phase) were set at the same level as that used before study commencement.

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Frequency (8 Hertz [Hz]), PEEP, mean airway pressure (MAP) and inspiratory to expiratory ratio (1:1) were not adjusted. The oscillatory amplitude was set at 20 centimeters of water (cm H_2O) at the outset of the study and modified to maintain transcutaneous carbon dioxide levels between 40 and 60 millimeters of mercury. If the infant was normocapnic, the smallest amplitude to achieve visible chest wall vibration was used. Since infants were nursed in a prone position throughout the study, dorsal lung regions were considered non-gravity-dependent.

Data Collection

An ultrasound-gel coated textile electrode belt with 32 electrodes was fastened at the nipple level.(19) During each intervention period, four 10-minute EIT sequences were recorded with the SenTec BB^2 EIT device (SenTec AG, Landquart, Switzerland) at a frame rate of 48 Hz in a custom-built infant imaging package.(19, 20) For each sequence, the first 30 stable consecutive breaths of artifact-free tidal ventilation were identified and data extracted. Recordings were excluded from analysis if more than 3 electrodes had insufficient skin contact or if less than 30 consecutive breaths could be identified.

Data Analysis

Data were extracted and analyzed using ibeX (version 1.1, SenTec AG, Landquart, Switzerland) and Matlab software (version 2019a, Mathworks, Nantick, MA, USA). First, predefined anatomical lung regions based on the vendor-provided human model chest atlas were projected into the EIT image and EIT signals outside of these regions excluded.(21, 22) Second, two bandpass filters were applied on all recordings (nHFOV and nCPAP) to split the unfiltered ventilation signal (ΔZ) into a signal for tidal breathing (ΔZ_{Spon}) and a signal for

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oscillations (ΔZ_{Osc}). A low-pass frequency of 3 Hz was used to isolate ΔZ_{Spon} from ΔZ; being three harmonics of the median respiratory rate of 59 breaths per minute during the recordings.(23, 24) We isolated the oscillatory signal (ΔZ_{Osc}) by applying two band-pass filters with a width of $\pm$ 0.2 Hz around 8 Hz (corresponding to the set frequency during nHFOV) and 16 Hz (the second harmonic of the nHFOV frequency). Third, for each of the two filtered signals, the amplitudes were extracted, averaged over the selected 30-breaths sequence, and normalized for body weight. Depending on the applied filter, this corresponded to the relative tidal volume (V_T) or the V_{Osc} (expressed in Arbitrary Units/kg [AU/kg]), respectively. Next, the V_{Osc}/V_T ratio was calculated for each recording. Fourth, regional ventilation distributions were quantified by assessing V_{Osc}, V_T and the V_{Osc}/V_T ratio separately for the gravity-dependent, non-gravity-dependent, right, and left lung. These relative changes in regional ventilation were then weighted to the known pixel contribution of each region to normalize for differences in lung size.(25, 26) Finally, functional EIT images (per patient and overall) were generated to visualize differences in the regional ventilation distribution between the tidal breathing signal and the oscillatory signal. The regional ventilation pattern of the tidal breathing signal was generated by subtracting the EIT signal at the start of inspiration from the signal at the end of inspiration. For the oscillatory signal, functional EIT images were generated using the standard deviation of the impedance time course.(17)

Statistical Analysis

Analyses were performed on the averages of each EIT recording. Normally distributed data are presented as mean with standard deviation (SD) or 95% confidence interval (CI). Non-parametric data are presented as median and interquartile range (IQR). Since each subject

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was measured four times during each mode of ventilation, comparisons between nHFOV and nCPAP were performed using a mixed model analysis of variance controlling for within-subjects variance (using the "afex" package in R statistics, version 3.6.2).(27) Correlation was assessed using Pearson's correlation coefficient. P-values < 0.05 were considered statistically significant.

Results

Population

Among 30 infants, 228 EIT recordings containing 6,840 breaths were analyzed, 112 recordings during nHFOV and 116 during nCPAP (Figure 1). Demographic and clinical characteristics of the included infants are provided in Table 1.

Frequency Spectrum

The unfiltered ventilation signals of one typical infant's recording and its corresponding frequency spectra are provided in Figure 2. During nHFOV, three frequency ranges can be identified. Areas shaded in green represent tidal breathing and areas shaded in red represent oscillations. The high-frequency spikes were not present during nCPAP.

Tidal and Oscillatory Volumes during nCPAP and nHFOV

The global tidal and oscillatory volumes during both modes of ventilation are provided in Table 2. The filtered ventilation signals ΔZ_{Spon} and ΔZ_{Osc} of one typical nCPAP and nHFOV recording are shown in Figure 3, A1/A2 and B1/B2. During nHFOV, V_{Osc} could be measured within the lungs with a mean (SD) tidal amplitude of 1.7 (1.0) AU/kg. The corresponding mean (SD) V_T was 9.5 (4.8) AU/kg, and the mean (SD) V_{Osc}/V_T ratio was 0.20 (0.13).

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Reassuringly, there was very little signal within the ΔZ_{Osc} domain during nCPAP. The mean (SD) oscillatory amplitude set at the ventilator was 20 (3.2) cm H_2O, which did not correlate with the measured V_{Osc} (r=0.13, *p*=0.18).

Regional Ventilation Patterns during nHFOV

The regional distributions of V_T and V_{Osc} expressed as total volumes, as percentage and as a ratio to account for anatomical sizes of lung regions is shown in Table 3. The non-gravity-dependent and the right lung contributed a greater portion to total V_T (Figure 3, B3 and Table 3). Similarly, oscillations were more likely to be transmitted to the non-gravity-dependent and right-sided lung regions (Figure 3, B4 and Table 3). The mean V_{Osc}/V_T ratio was higher in the non-gravity-dependent compared with the gravity-dependent lung [mean difference (95% CI): 0.041 (0.025 to 0.058); *p*<0.001] and higher in the right compared with the left lung [mean difference (95% CI): 0.040 (0.019 to 0.061); *p*<0.001]. There was no change in the ventilation homogeneity ratio with different amplitudes in all four lung regions (see Table E1 in the online data supplement). Regional oscillation and ventilation maps for each individual patient are available online (see Figure E1 in the online data supplement).

Discussion

The mechanisms by which the clinical benefits of nHFOV are mediated are largely unknown. With this study, we provide the first evidence of substantial transmission of oscillatory volumes into the lung of preterm infants on nHFOV support. We also demonstrate that compared with the regional distribution of tidal breaths, oscillations are more likely to reach the right and the non-gravity-dependent areas of the lung.

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Noninvasive HFOV was developed to combine the advantages of endotracheal HFOV and noninvasive ventilation.(2, 3) It is thought that the oscillations during nHFOV deliver a small tidal volume, thereby eliminating CO_2 mostly from the upper airways and adding to CO_2 clearance by tidal breathing from the lower airways.(28, 29) During nHFOV, however, gas could theoretically also be transported to the distal parts of the lung by other mechanisms including convective flow, longitudinal dispersion due to turbulence, and pendelluft, depending on the respiratory cycle.(10–13, 30) Moreover, oscillations during nHFOV are known to be dampened by various mechanisms, which may explain that thoracic movements attributed to oscillations were only marginal in four one-year old infants.(15, 31) In contrast to these older infants, the highly compliant chest wall in preterm infants facilitates pressure transmission during nHFOV. Furthermore, respiratory inductance plethysmography measures the movement of the chest and abdominal wall and can only approximate the actual oscillatory volume transported to the alveoli. By measuring EIT changes in regional ventilation distribution, we demonstrated that contrary to previous suggestions, nHFOV oscillations are transmitted to the lung level in preterm infants. In fact, the oscillations' amplitude was approximately a fifth of the overall tidal volume during nHFOV, which would correspond to an absolute oscillatory volume of 0.8 – 1.2 ml/kg with regards to the internationally recommended total tidal volume for ventilated preterm infants.(32) Thus, our data suggest that CO_2 removal during nHFOV may also occur in the intrathoracic airways.

We also found that during each inflation, overall tidal volumes within the lung were comparable for both interventions, although V_T was lower during nHFOV. This may support the use of higher MAPs to facilitate gas exchange when escalating infants from nCPAP to

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nHFOV, but this has not yet been evaluated in adequately powered clinical trials.(7) One could speculate that infants on nHFOV may need to work less hard than infants on nCPAP support to achieve the same gas exchange, however, this is difficult to quantify. Furthermore, the lower V_T during nHFOV may provide a potential explanation for the finding in the original trial that infants on nHFOV required more oxygen to remain within the oxygen saturation target.

We did not observe a correlation between the amplitude set at the ventilator and the V_{Osc} reaching the lung. However, the amplitude during the study was increased until there was a visible wiggle of the infant's thorax. We speculate that due to intrinsic variations in compliance and resistance, different amplitudes may have been required to achieve the same V_{Osc} reaching the infant's lung.(33)

Clinical studies suggest that nHFOV may be better than nCPAP for post-extubation support and respiratory stability, particularly in preterm infants with evolving BPD.(4–7) Our physiological data support these findings and offer potential explanations for the clinical benefits of nHFOV. Since inspiratory glottic dilator activity seems to be maintained during nHFOV,(34) we speculate that in contrast to pressure peaks during non-synchronized noninvasive positive pressure ventilation, oscillations may be transmitted to the lung more consistently.(35) This may provide a continuous stimulus and a possible explanation for the clinical benefit of nHFOV.

The regional distribution of oscillations during nHFOV has never been described before. We found that compared with V_T, V_{Osc} are more likely to be transmitted to the right lung. The angle of the tracheal bifurcation is more acute for the left main bronchus compared with the right, and this difference is more pronounced in infants than in adults.(36–38) The more

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acute angle might dampen the transmission of oscillations to the left side,(11, 12, 39) and this effect may be frequency-dependent.(14) Altered flow profiles during the higher oscillatory frequency may explain the differences in ventilation distribution compared with frequencies of regular tidal breathing.(10–12) During tidal breathing there is mainly quasi-steady flow whereas during HFOV there are various factors contributing to gas exchange.(10, 40) Miedema and colleagues found that a similar increase in pressure amplitude during endotracheal HFOV resulted in a significantly greater increase of oscillatory volume in the right compared with the left lung.(41)

Interestingly, V_{Osc} were also transmitted predominantly to the non-gravity-dependent parts of the lung and in fact, this effect was greater than during tidal breathing. As infants were prone throughout our study, the non-gravity-dependent lung regions correspond to the dorsal parts of the lung. The angle of the dorsal diaphragm is steeper compared with the ventral diaphragm, potentially contributing to higher V_T in the dorsal lung. Oscillatory gas flow, however, also consists of diaphragm-independent mechanisms such as pendelluft or turbulent longitudinal dispersion.(30) Thus, the predominant transmission of V_{Osc} to the non-gravity-dependent lung region may be due to frequency-dependent effects: Recently, it had been shown in sheep that ventilation in the non-gravity-dependent lung was higher with an increasing oscillatory frequency.(14) Due to gravitational forces, the non-gravity-dependent lung has a higher compliance which leads to more volume delivered to these lung units.(42) This effect is even more pronounced for higher frequencies. (42, 43) We hypothesize that these mechanisms may contribute to an increased regional ventilation homogeneity, which may ultimately lead to a decrease in preterm lung injury during nHFOV.(44, 45) While our results are intriguing from a physiological perspective, high-

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quality evidence from larger randomized controlled trials demonstrating a lasting clinical improvement is still lacking. We think that currently, nHFOV may be justified on a case-by-case basis to avoid intubation.

Our study has several limitations. First, we studied a small sample of infants. However, even with only 30 infants we had 228 separate EIT recordings and 6,840 breaths to evaluate, thus increasing the value of the dataset. Importantly, we showed that, in contrast to studies of different populations, oscillations during nHFOV are transmitted to the lung level in stable preterm neonates. The distribution pattern was similar for most infants, strengthening the validity of our results. Second, EIT measures relative changes, thus, we cannot draw conclusions regarding the absolute volume changes in the lung during nHFOV. However, EIT measurements have been proven to correlate well with measured tidal volumes in animal studies (46, 47) and are representative of the whole lung in ventilated preterm infants.(18) Third, a single ventilator model was used to deliver nHFOV. Since the type of ventilator may impact the performance of nHFOV, our results cannot be extrapolated to other devices.(48)

Conclusion

In preterm infants, oscillatory volumes during nHFOV are transmitted to the lung. Compared with the regional distribution of tidal breaths, oscillations preferentially reach the right and non-gravity-dependent lung. These data increase our understanding of the physiological processes underpinning nHFOV and may lead to further refinement of this novel technique.

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Figure legends

Figure 1.

Flowchart of infants and recordings analyzed during this study.

Figure 2.

Raw EIT signals of one exemplary nCPAP and nHFOV recording on the left with its corresponding frequency spectrum on the right. During nHFOV, there are clearly detectable frequency spikes at 8 Hz and 16 Hz (red shaded areas), which are not present during nCPAP.

Figure 3.

Tidal breathing and oscillatory signal of one exemplary nCPAP and nHFOV recording after application of a frequency filter at ≤3Hz (A1 and B1) and two bandpass filters at 8 Hz and 16 Hz (A2 and B2). Parts B3 and B4 show the corresponding regional ventilation distribution over all patients during nHFOV pixel-by-pixel (lighter blue corresponding to a stronger change in EIT signal) and as fraction of ventilation in 36 slices, as mean + SD: Numbers show the percentage of ventilation in the corresponding quadrants. Since infants were nursed in a prone position throughout the study, functional EIT images are shown in a dorsal-ventral orientation. Thus, ventral lung regions (i.e. those closest to the mattress pictured as a thick grey line) were considered gravity-dependent. Oscillatory volumes were shifted towards the right and non-gravity-dependent lung regions. Abbreviations: GD = gravity-dependent lung, NGD = non-gravity-dependent lung, L = left lung, R = right lung.

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Tables

Table 1. Baseline Demographics and Clinical Characteristics

Characteristics	Median (IQR)
Perinatal	
Gestational age at birth, wks	26.6 (25.6 – 27.3)
Birth weight, g	870 (772 – 1,020)
Male, n (%)	16 (53)
Antenatal glucocorticoids, n (%)	26 (87)
Apgar score at 5 minutes	8 (6 – 8)
Exogenous surfactant, n (%)	29 (97)
Before randomization	
Endotracheal ventilation, n (%)	29 (97)
Duration of endotracheal ventilation, days	11 (2 – 31)
Duration of noninvasive ventilation, days	12 (9 – 19)
Postnatal glucocorticoids, n (%)	11 (37)
At randomization	
Postnatal age, days	33 (16 – 45)
Postmenstrual age, wks	31.1 (30.0 – 32.0)
Weight, g	1271 (1069 – 1583)
Nasal CPAP pressure, cm H_2O	7 (6 – 8)
FiO_2	0.30 (0.28 – 0.34)
SpO_2/FiO_2	300 (263 – 321)
Capillary blood gas	
pH	7.35 (7.33 – 7.39)
pCO_2, mmHg	53 (48 – 57)

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Base excess, mmol/l	2 (-1 – 4)
HCO_3-, mmol/l	28 (26 – 32)
Respiratory follow-up	
Bronchopulmonary Dysplasia, n (%)*	21 (70)

Depicted as median and interquartile range, except where otherwise specified.

*Bronchopulmonary Dysplasia was diagnosed at 36-weeks corrected gestation according to the modified Walsh criteria.(49)

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Table 2. Global Tidal and Oscillatory Volumes during both Modes of Ventilation.

	CPAP	HFOV	Mean difference (95% CI)	Test statistic*
V_T [AU/kg]	11.6 (5.0)	9.5 (4.8)	2.1 (0.8 to 3.4)	F=33, p<0.001
V_{Osc} [AU/kg]	0.1 (0.1)	1.7 (1.1)	-1.6 (-1.4 to -1.8)	F=413, p<0.001
V_{Osc}/V_T Ratio	0.01 (0.01)	0.20 (0.13)	-0.19 (-0.16 to -0.21)	F=333, p<0.001

Analyses are based on the averages of each EIT recording. *The F value is the test statistic of the analysis of variance and corresponds to the variation between subjects divided by the variation within subjects. P-values of the mixed model analysis of variance are shown. Abbreviations: V_T = Tidal volume; V_{Osc} = oscillatory volume; V_{Osc}/V_T ratio = ratio of oscillatory volume divided by tidal volume.

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Table 3. Regional Ventilation Distribution of Tidal and Oscillatory Volumes during nHFOV

	V_T			V_{Osc}		
	EIT signal [AU/kg]	Ventilation distribution [%]	Ventilation homogeneity ratio*	EIT signal [AU/kg]	Ventilation distribution [%]	Ventilation homogeneity ratio*
Overall	9.5 (4.8)			1.7 (1.1)		
Right	6.2 (4.0)	63 (22)	1.14 (0.37)	1.1 (0.8)	65 (19)	1.15 (0.32)
Left	3.3 (1.7)	37 (15)	0.95 (0.38)	0.6 (0.4)	35 (18)	0.90 (0.45)
NGD	5.4 (2.7)	57 (10)	1.04 (0.19)	1.0 (0.7)	62 (7)	1.11 (0.13)
GD	4.1 (2.3)	43 (13)	0.99 (0.29)	0.7 (0.4)	38 (7)	0.87 (0.16)

All data are shown as mean (SD). *The ventilation homogeneity ratio corresponds to the relative changes in regional ventilation which were weighted to the known pixel contribution of each anatomical lung region: The percentage of tidal volume (V_T) and oscillatory volume (V_{Osc}) reaching the respective part of the lung was divided by the anatomical lung size of the right, left, non-gravity-dependent and gravity-dependent parts of the lung. A value greater than 1 means the amount of V_T or V_{Osc} in that region is greater than the anatomically expected contribution of that region. Abbreviations: NGD = non-gravity-dependent, GD = gravity-dependent.

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Figure 1

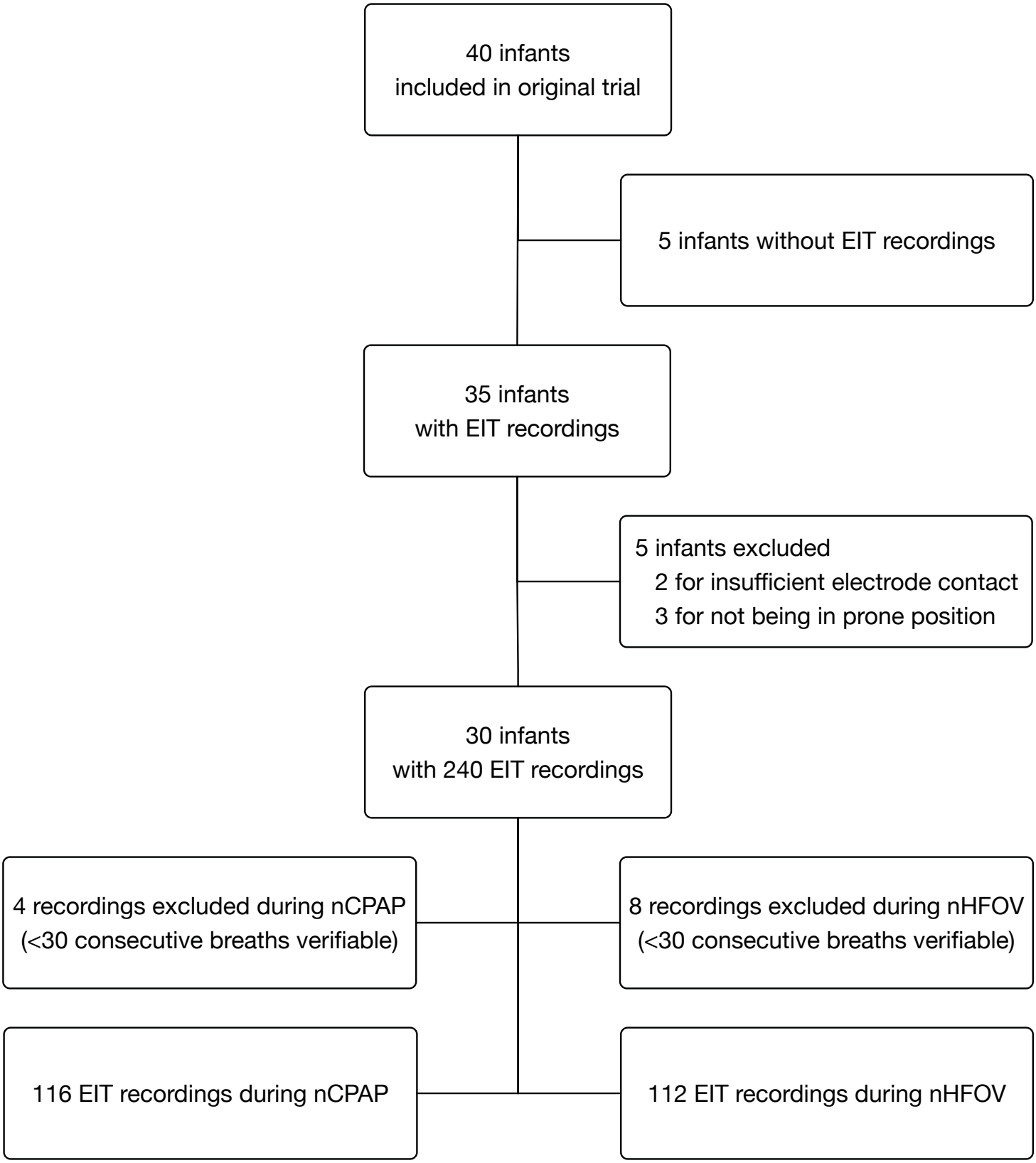

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Figure 2

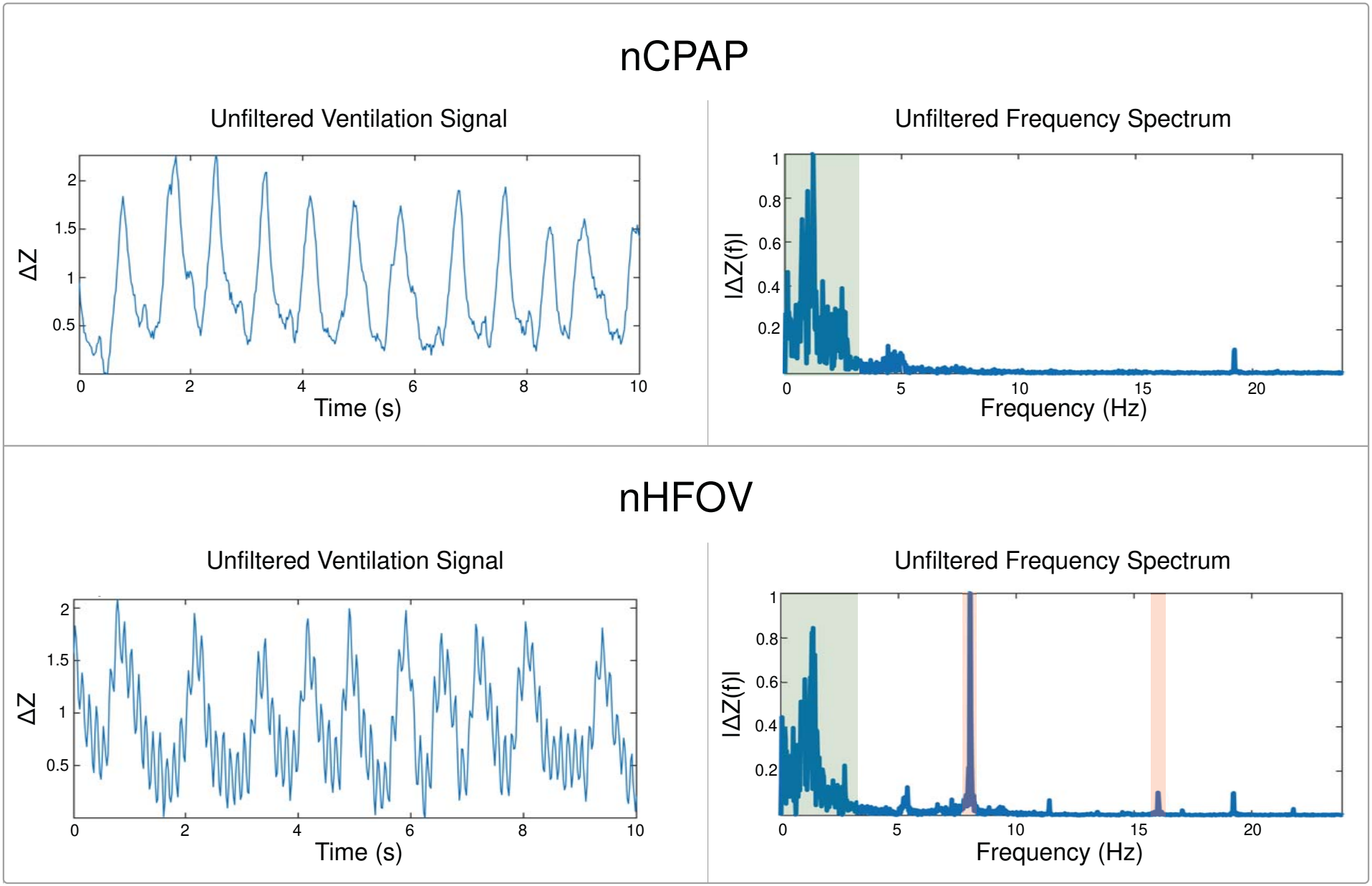

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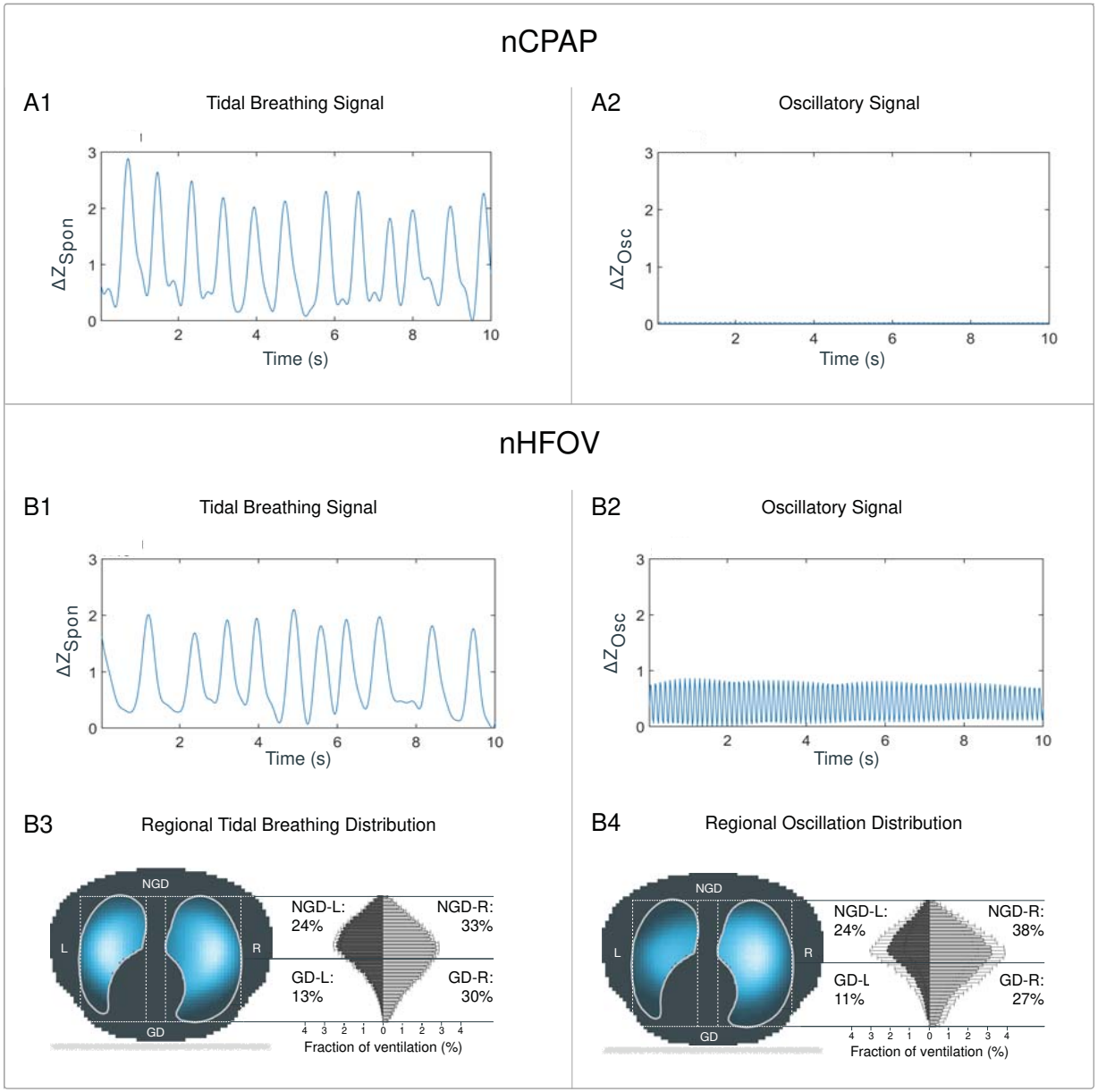
Figure 3



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Transmission of Oscillatory Volumes into the Preterm Lung during Noninvasive High-Frequency Ventilation

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Online Supplemental Material

Supplementary Data

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Table E1: Changes in ventilation homogeneity ratio by level of amplitude

Lung regions	Amplitude				Test statistic*
	10-14 cm H_2O (n=8)	15-19 cm H_2O (n=21)	20-24 cm H_2O (n=74)	>25 cm H_2O (n=9)	
Gravity-dependent	0.78 (0.13)	0.84 (0.12)	0.87 (0.17)	1.02 (0.15)	F=1.02, p=0.32
Non-gravity-dependent	1.19 (0.14)	1.13 (0.10)	1.11 (0.14)	0.98 (0.12)	F=2.19, p=0.15
Right	0.74 (0.34)	1.09 (0.26)	1.17 (0.31)	1.47 (0.15)	F=2.34, p=0.13
Left	1.54 (0.61)	0.92 (0.39)	0.88 (0.39)	0.41 (0.21)	F=3.47, p=0.07

Mean (SD) ventilation homogeneity ratio in all four lung regions along the non-gravity-dependent to dependent and the right to left axis. Amplitudes were arbitrarily divided into four groups to allow adequate statistical analysis (n≥5 in each group). *A mixed model analysis of variance controlling for within-subjects variance was used.

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Figure E1: Individual regional tidal breathing and oscillatory distribution during nHFOV

Tidal breathing and oscillatory functional EIT (fEIT) image of the ventilation-related changes within the right and left lung for each of the 28 preterm infants for whom EIT recordings during noninvasive high-frequency oscillatory ventilation were available. Relative tidal ventilation is represented with a blue heat-map scale with black (no ventilation) to white (maximum). Since infants were nursed in a prone position throughout the study, fEIT images are pictured in a dorsal-ventral orientation. Thus, ventral lung regions (i.e. those closest to the mattress) were considered gravity-dependent.

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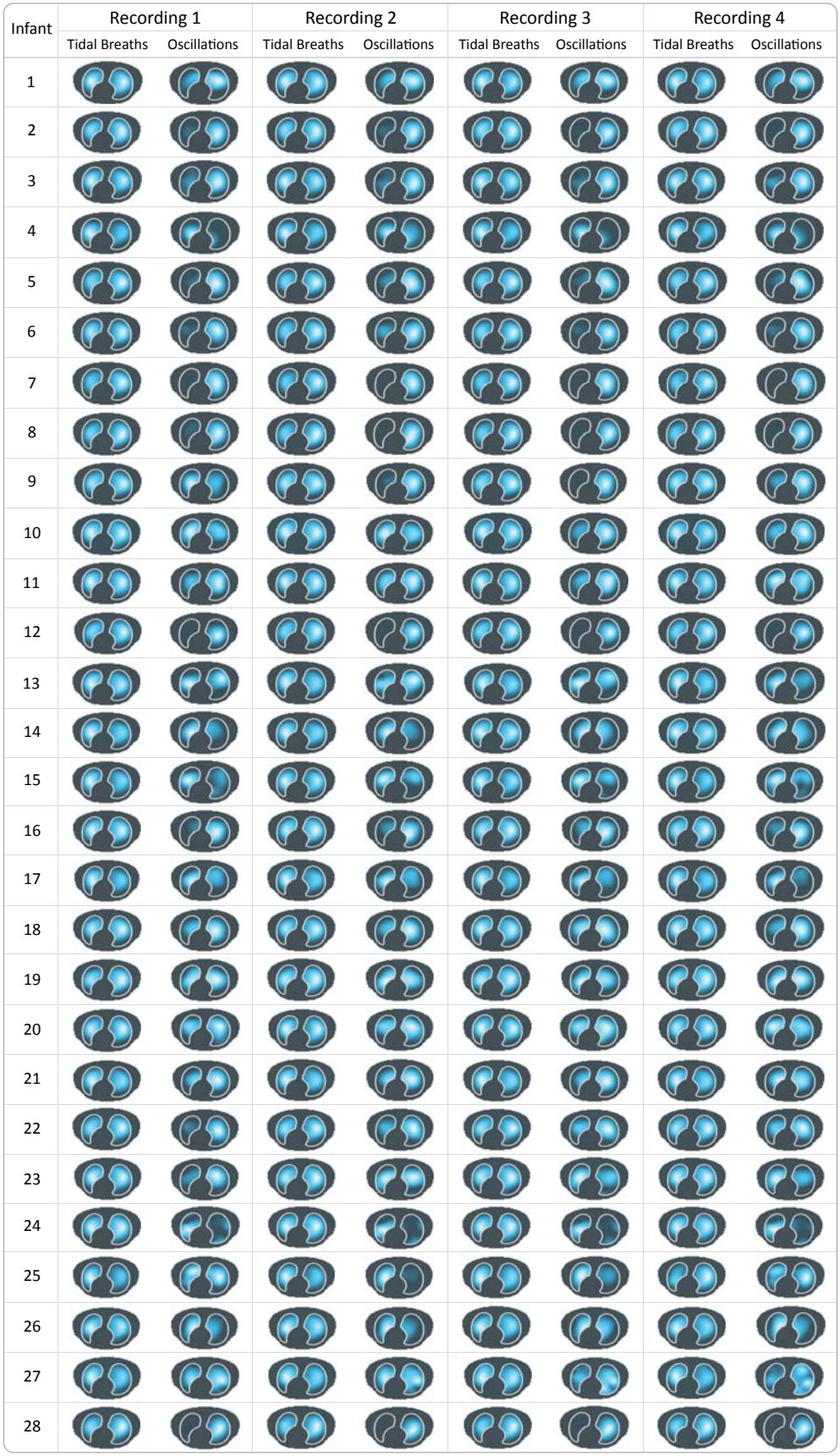
Figure E1



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